

A HYDROGEL-ACTUATED SMART MICROVALVE WITH A POROUS DIFFUSION BARRIER BACK-PLATE FOR ACTIVE FLOW CONTROL

Antonio Baldi ¹, Yuandong Gu ², Paul E. Loftness ³, Ronald A. Siegel ², Babak Ziaie ¹

¹Department of Electrical and Computer Engineering, ²Department of Pharmaceutics and ³Department of Mechanical Engineering, University of Minnesota, Minneapolis, MN 55455. E-mail: baldi@ece.umn.edu

ABSTRACT

This paper reports on the fabrication and testing of a hydrogel-actuated microvalve that responds to changes in the concentration of specific chemical species in an external liquid environment. It consists of a hydrogel disc sandwiched between a porous plate and a flexible silicone rubber membrane. Swelling of the hydrogel produced by diffusion of chemical species through the porous plate results in the deflection of the membrane and closure of the valve intake orifice. A phenylboronic acid based hydrogel was used to construct a smart microvalve that opens and closes in response to the changes in the glucose concentration and pH. The fastest response time achieved was 16 minutes using a 70 μm thick hydrogel and a 60 μm porous back plate.

INTRODUCTION

Environmentally sensitive hydrogels offer unique opportunities for active flow control in microflow systems [1]. These tangled networks of cross-linked polymer chains, immersed in a solvent, manifest a reversible and abrupt swelling phase transition in response to changes in environmental factors such as glucose concentration, pH, electric field, temperature, and light. This transition often results in an abrupt volume change (swelling or shrinking) that can be as large as 1000 fold or more. Because of this property, hydrogels are attractive candidates as components of microactuators operating in aqueous media such as body fluids. For example, the volume phase transition in these materials can be harnessed in smart microfluidic components.

The volume change behavior of hydrogels is diffusion-limited, and therefore exceedingly slow when the diffusion pathlength is large ($\tau=L^2/D$, where τ is the time constant, L is a critical dimension, and D is the diffusion constant). In certain microscale applications, the absorption and expulsion of solvent is sufficiently fast to permit hydrogels to be used as mechanical actuators with a reasonable response time (<1 minute). MEMS-based hydrogel actuators are among such applications. Integrating hydrogels with MEMS microfluidic structures such as valves and pumps can provide smart

microsystems that respond to various environmental stimuli. Several different approaches have been proposed to accomplish this goal. Hydrogels have been selectively photopolymerized around posts inside silicon microchannels to regulate flow in response to the changes in the flowing solution [2]. Alternatively, hydrogels have been polymerized along a pair of silicone flaps attached to the walls of a microchannel forming a structure mimicking venous valves [3]. Flow inside a microchannel has also been controlled by the concentration of the solution flowing in an adjacent microchannel [2]. In this case the channels were separated by a silicone rubber membrane, whose deflection by volume changes of the hydrogel placed in one channel produced the opening and closing of an inlet hole in the other channel.

All the aforementioned techniques control flow in response to the changes in the concentration of a solution inside a microchannel. A recent design intended for drug delivery applications provides external exposure through a perforated plate [4]. However, that device is large (macromachined from methacrylate plates) and hence its response is exceedingly slow (~10 hours response time). In this paper we describe the fabrication and testing of a microvalve capable of responding to changes in concentration of an external solution surrounding the device. In our approach the hydrogel is placed in a cavity that communicates with the external solution by diffusion through a stiff porous plate. The hydrogel volume change produces deflection of a bossed membrane that opens and closes the intake orifice of the valve. Applications of this unique approach are obvious in the field of drug delivery microsystems and biotechnology. Devices can be easily designed to deliver drugs or other chemicals on demand. In subsequent sections, we will describe the design, fabrication, and testing of the glucose-sensitive microvalve.

DESIGN AND FABRICATION

Figure 1 shows the cross-sectional schematic of the microvalve. The valve consists of a silicone rubber membrane with a central silicon boss, which can open or close an intake orifice drilled into a glass substrate. Low

modulus silicone rubber is used as the membrane material in order to provide large deflections (hundreds of microns) in response to the volume change in the hydrogel. The hydrogel is trapped in a cavity sandwiched on the top by a porous stiff plate, and on the bottom by the silicone rubber membrane. The top porous plate allows the diffusion of small molecules such as water, glucose, and urea, while providing a mechanical support for the hydrogel and preventing its escape from the cavity. This unique arrangement allows the microvalve to respond to external environmental stimuli.

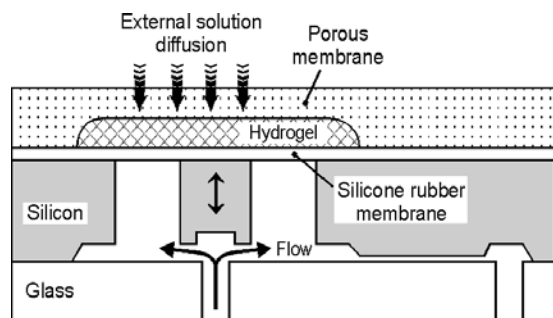


Figure 1: Schematic drawing of the valve cross-section and working principle.

Dimensions of the hydrogel cavity are a key point in obtaining a short response time. The porous back-plate should be thin enough to allow fast diffusion while at the same time provide enough mechanical stiffness against the hydrogel swelling. As was mentioned previously, the response time of the hydrogel depends quadratically on its thickness. Therefore, in order to achieve short response times one needs to use a very thin hydrogel. On the other hand, the thinner the hydrogel, the smaller the amount of its work output. A low Young's modulus membrane such as silicone rubber can be used to counteract this and obtain large deflections with small pressures. In the present design a bossed silastic membrane was used to open and close an intake orifice. The diameter of the membrane and central boss was 1800 μm and 500 μm respectively.

Figure 2 shows the fabrication process of the microvalve. An initial KOH etch on a silicon wafer is used to define: 1) the gap between the boss and the intake orifice, and 2) a V-shaped microchannel connecting the intake to the output orifice (2-a). Subsequently the valve seats are defined in the recess using a dry etching step (2-b). A flexible silastic membrane is then spin-casted on the unpolished side of the silicon wafer. A two component silicone rubber (Nusil MED10-6640) is spun at 1000 rpm for 20 seconds and cured for 30 minutes at room temperature, 45 minutes at 75 $^{\circ}\text{C}$ and 135 minutes at 150 $^{\circ}\text{C}$, resulting in a final thickness of 20 μm . Finally, a deep RIE step is used to remove the silicon under the membrane and create the central boss (2-c). A Pyrex[®] glass substrate containing the ultrasonically drilled inlet

and outlet orifices (250 μm diameter) is fabricated separately (2-d).

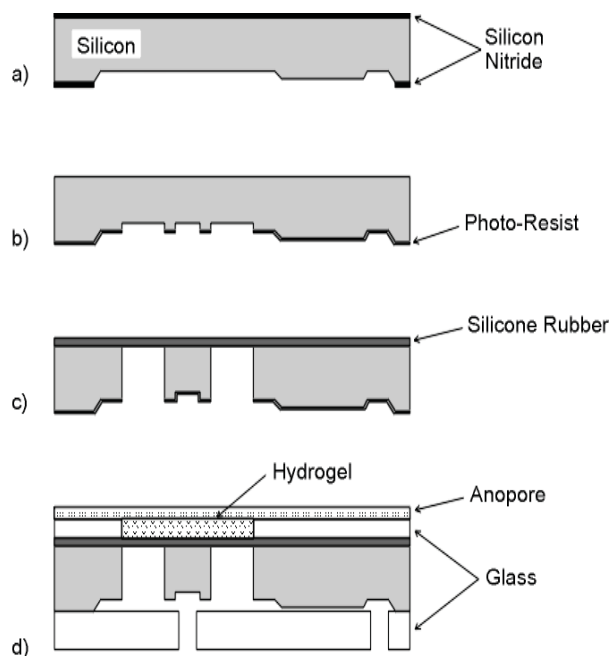


Figure 2: Fabrication process. a) KOH etch (valve gap and microchannel definition), b) First deep RIE (valve seats definition), c) Silicone rubber spinning and second deep RIE (membrane release and boss definition), d) Assembled valve with Anopore[™] porous back-plate.

The first KOH step is critical in defining the gap between the boss and the intake orifice. This separation defines the membrane deflection that the hydrogel needs to produce in order to close the valve. The results presented in this paper were obtained from valves with 70 μm KOH etch depth. As was mentioned previously, the step also defines a V-shaped microchannel that fixes the flow rate in the open state to a predetermined value. The use of microchannels to obtain accurate dose rates has proved to be very reliable [5].

MICROVALVE ASSEMBLY AND HYDROGEL LOADING

The silicon substrate and the glass plate containing the inlet-outlet orifices are assembled using a UV curable epoxy. A simple transparency mask is used to avoid curing of adhesive inside the microfluidic area. Non-cured remaining adhesive is rinsed out in acetone. The hydrogel is cured inside a mold with suitable dimensions and is placed on top of the membrane prior to mounting the porous back-plate. The remaining parts (spacer, porous plate and connectors) can be assembled using a silicone-based adhesive. Figure 3 is a photograph of a completely assembled microvalve.

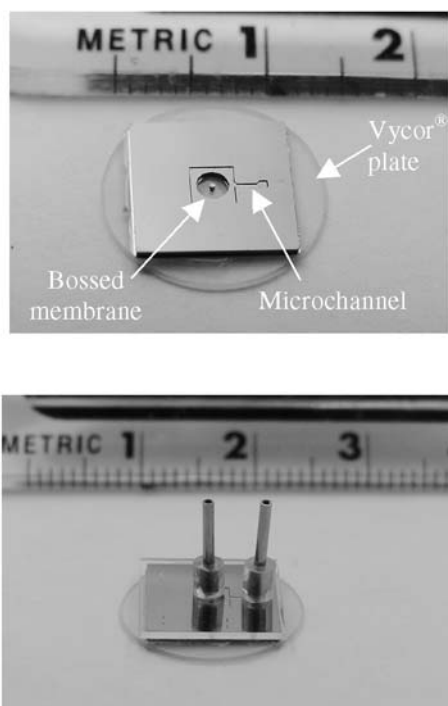


Figure 3: Silicon part and Vycor[®] back-plate assembled together (up) and completely assembled valve with microfluidic connectors (down).

TEST RESULTS AND DISCUSSION

A schematic drawing of the experimental setup used to test the microvalve is shown in Figure 4. The test liquid was deionized water and the inlet pressure was produced from a water column having a constant height. The pressure drop between inlet and outlet during the measurements was 6 kPa. The flow rate was measured from the velocity of an air bubble injected in a capillary connected to the outlet. The valves were alternatively immersed in solutions of different analyte concentrations allowing them to fully open and close before switching from one solution to the other. A magnetic stirrer was used to assure homogeneity of the solution.

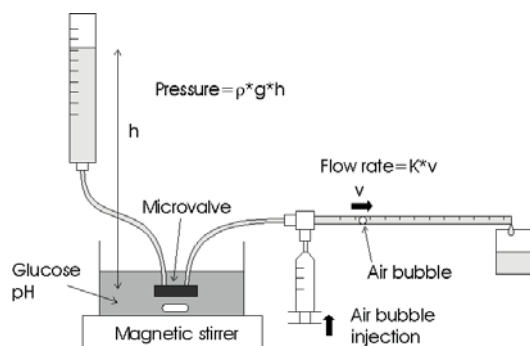


Figure 4: Experimental setup showing the water column, glucose bath, and air bubble flow meter.

Two different materials were tested as the porous stiff plate. These were, Anopore[™] aluminum oxide (1000 Å pore size and 60 μm thickness), and Vycor[®] 7930 porous glass (40-200 Å pore size and 500 μm thickness). Vycor[®] can be mechanically machined (ultrasonic milling) or chemically etched (HF:HNO₃:H₂O, 3:7:10) to form the cavity where the hydrogel is placed. Alternatively, the Vycor plate can be thinned down using chemical etching to decrease the diffusion path length. For the Anopore[™] back-plate, glass cut with a circular hole can be placed between the silicone membrane and the porous plate to create the cavity (Figure 2-d). The assembly of the microvalve was simplified for test purposes by mechanically clamping together the different substrates. For very thin hydrogel pieces (<100 μm) the glass spacer was not necessary since the deflection caused by the hydrogel volume in the shrunken state was small enough to keep the valve open.

Figure 5 shows the silicone rubber membrane deflection measured before assembling the valve by applying a pressure at the external side and measuring the displacement of the silicon boss with an optical microscope. Deflections of up to 200 μm were obtained at pressures as low as 3 kPa. Figure 6 shows the behavior of the valve when an external pneumatic pressure controls the opening and closing. The hysteresis observed is due to the unequal surfaces seen by the liquid pushing the membrane on the inner side in the closed and open states. No leakage flow was detected in the closed state.

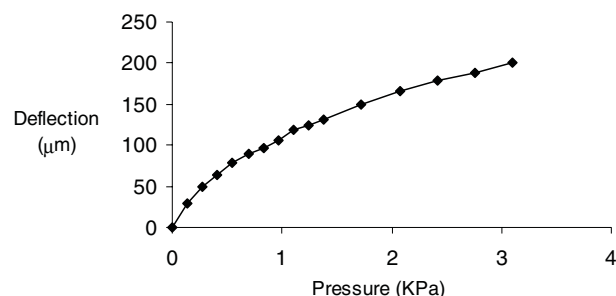


Figure 5: Deflection of the silicone rubber membrane with external pressure.

The complete valve behavior was tested using a phenylboronic-acid-based hydrogel [6]. This particular hydrogel is glucose- and pH-sensitive, and a valve containing this hydrogel can be used to regulate the flow of insulin in a drug delivery system in response to changes in glucose concentration. Figure 7 shows the response of the valve to changes in pH when an Anopore[™] back-plate and a 70 μm thick hydrogel were used. The valve was immersed alternately in two phosphate saline solutions with pH 7.4 and 10 (adjusted adding NaOH). A response time of about 16 minutes is observed.

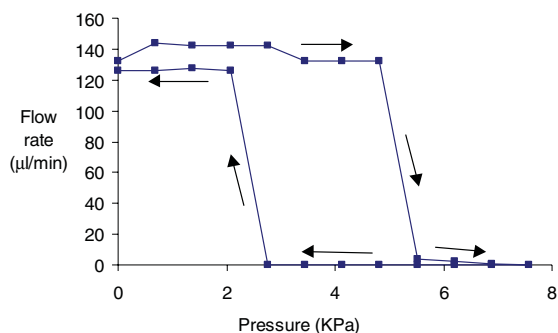


Figure 6: Valve flow rate when an external pressure deflects the membrane.

In Table 1 we summarize the results from experiments with different types of porous plates, hydrogel thicknesses, and solution conditions (pH or glucose concentration). The hydrogel thicknesses referred to are the ones of the mold in which they were cured. Response times were measured as the interval between a concentration change to the point when 50% of full-scale flow rate was reached. The fastest response (16 min) corresponds to the thinnest hydrogel and pH as the control signal. The faster response of pH-controlled valves is consistent with the fact that the diffusion coefficient of H^+ ion is higher than that of glucose. As mentioned previously, thickness of the hydrogel is also an important factor in the response time. However, we did not observe a quadratic dependence as is expected from a diffusion-controlled process. We believe this deviation is the result of: 1) additional time required for the diffusion of chemical species through the porous plate, and 2) neglect of binding/unbinding reactions between the analyte and the phenylboronic acid groups on the hydrogel.

Table 1: Response times for different porous plates, hydrogel thicknesses, and analytes. Glucose variations are between 0 and 20 mM. pH changes between 7.4 and 10.

Porous plate	Hydr. Thick	Analyte	Opening resp. time	Closing resp. time
Anopore™	500 μm	Glucose	4 h and 15 min	4 h and 20 min
Anopore™	70 μm	Glucose	32 min	18 min
Anopore™	70 μm	pH	16 min	18 min
Vycor® (100 μm thick)	70 μm	pH	90 min	56 min

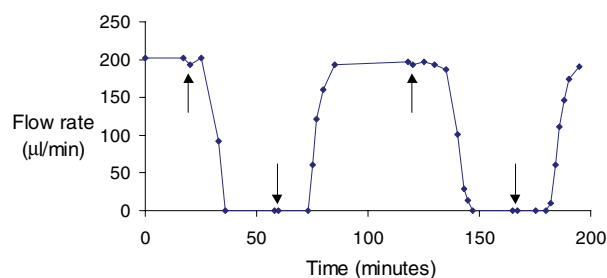


Figure 7: Flow rate during external solution pH changes. Downward arrows mark a change from pH 10 to pH 7.4. Upward arrows mark a change from pH 7.4 to pH 10.

CONCLUSIONS

In this paper, we reported on the design, fabrication, and testing of a smart hydrogel-based microvalve for active flow control in drug delivery and microfluidic applications. An environmentally sensitive hydrogel was sandwiched between a stiff porous back-plate and a flexible silicone rubber membrane. Exposure to an external variable environment (e.g., different glucose concentrations, pH) results in a reversible swelling-deswelling of the hydrogel, deflection of the silicone membrane, and closure of the valve intake orifice. Response times as low as 16 minutes were obtained using 70 μm glucose sensitive hydrogels.

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